



# Overcoming Chemoresistance Via Extracellular Vesicle Inhibition

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# INTRODUCTION



## Overcoming Chemoresistance via Extracellular Vesicle Inhibition

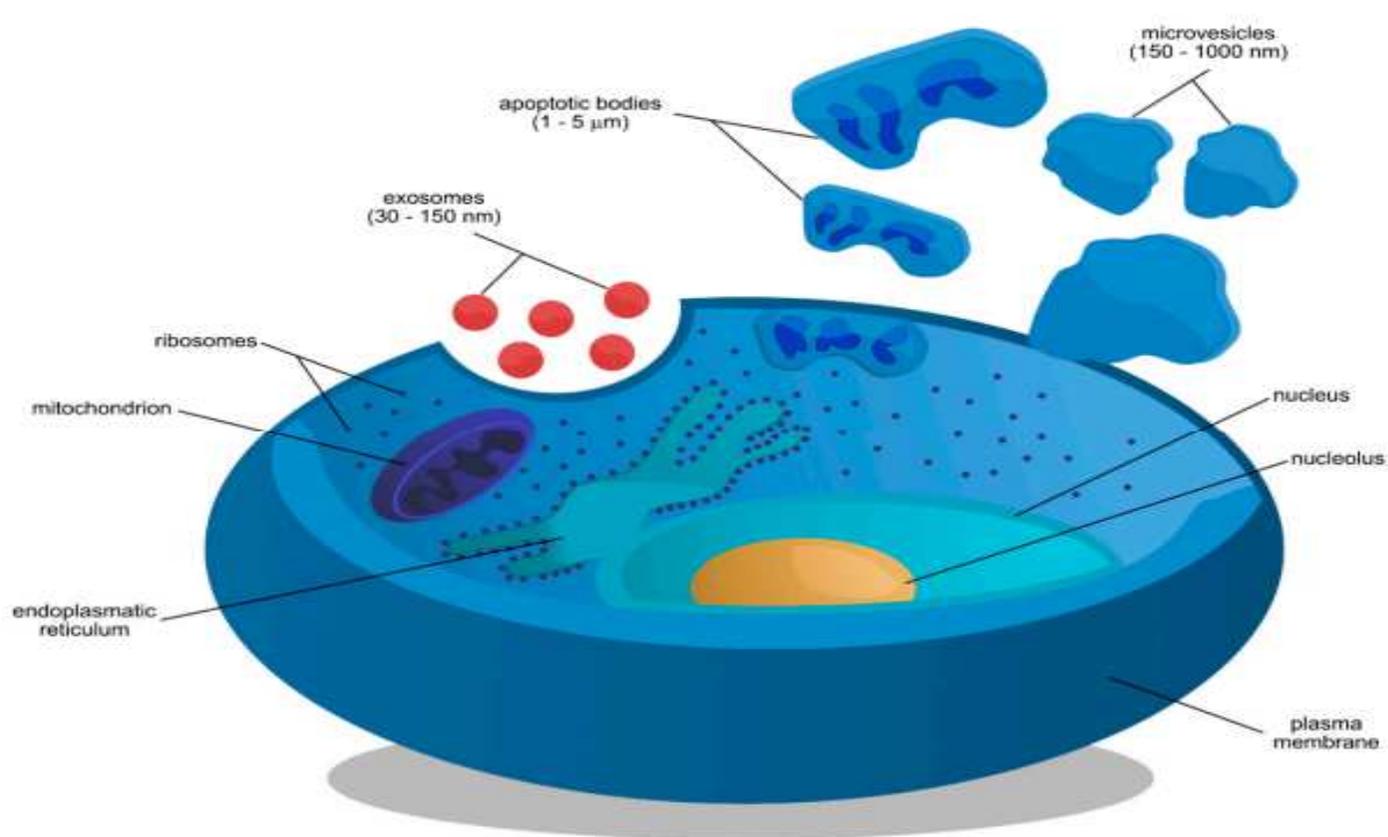
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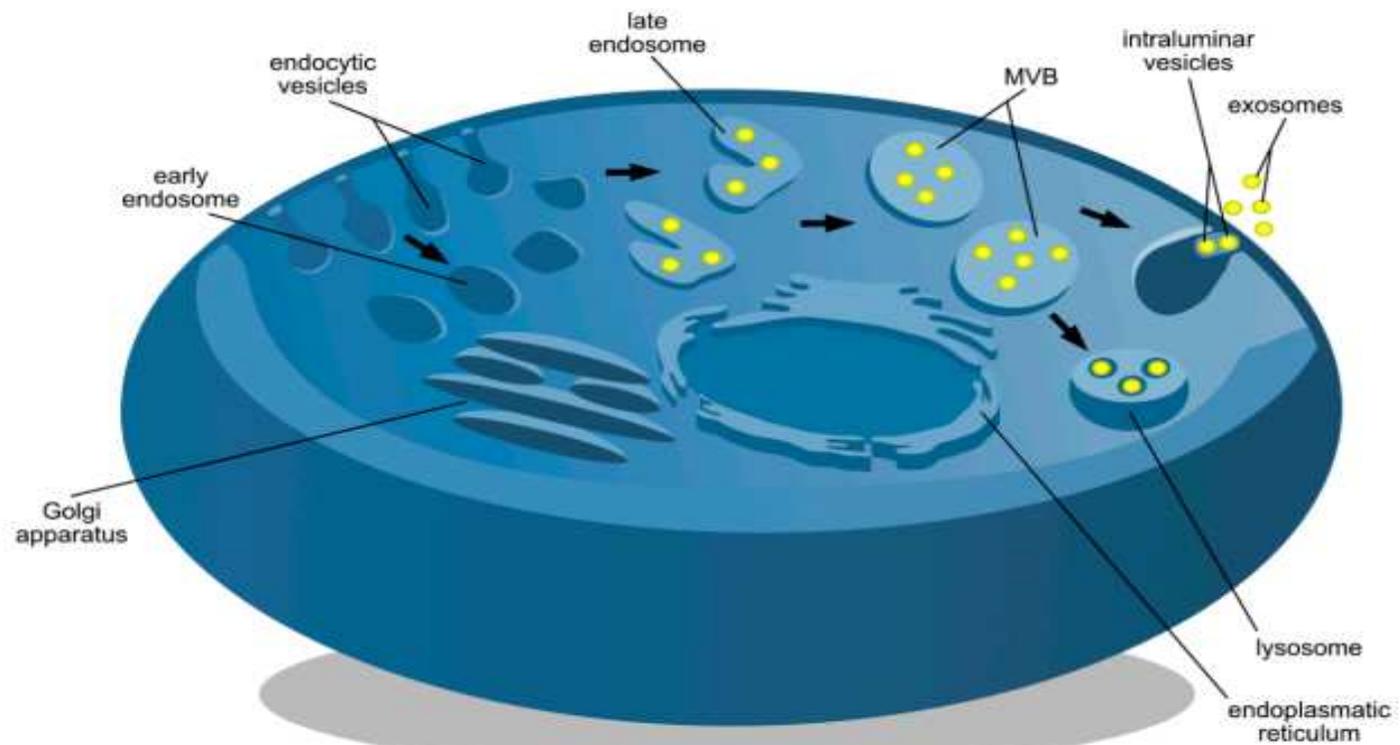
# IN A NUTSHELL

- SUBTYPES OF EVS
- BIOGENESIS AND RELEASE OF EVS
- UPTAKE OF EVS
- REGULATION OF CHEMORESISTANCE BY EVS
- INHIBITION OF EVS
- DIFFICULTIES, LIMITATIONS, AND CONSIDERATIONS IN EVS INHIBITION
- TARGETING EVS IN CLINICAL APPLICATIONS

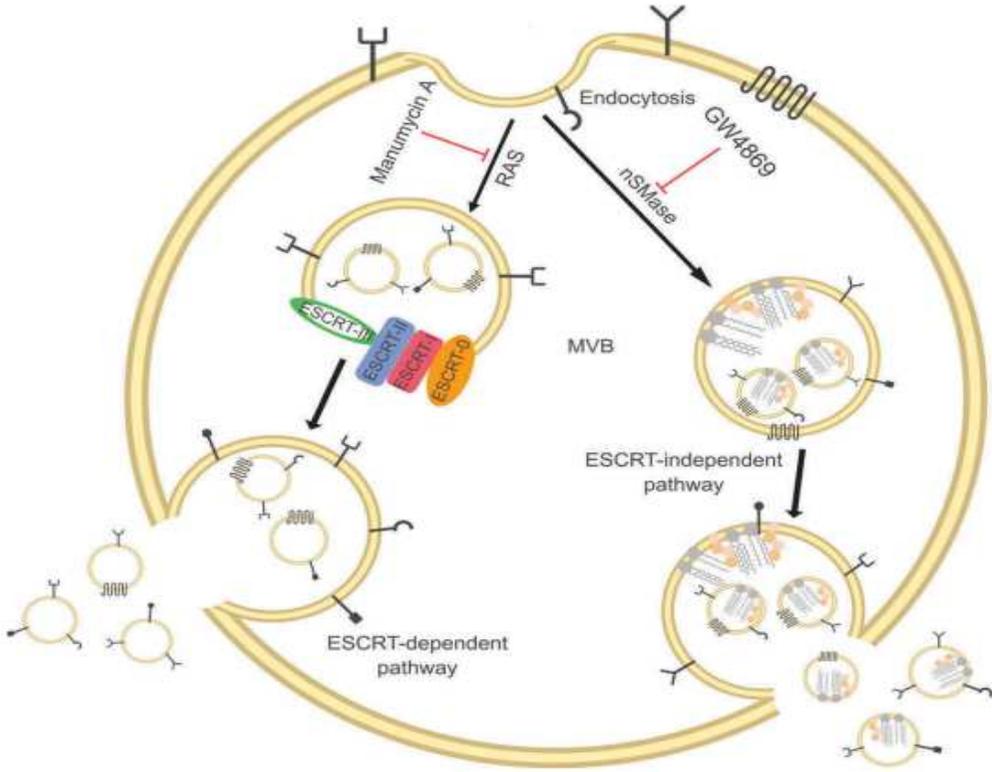
# SUBTYPES OF EVS



# BIOGENESIS AND RELEASE OF EVS



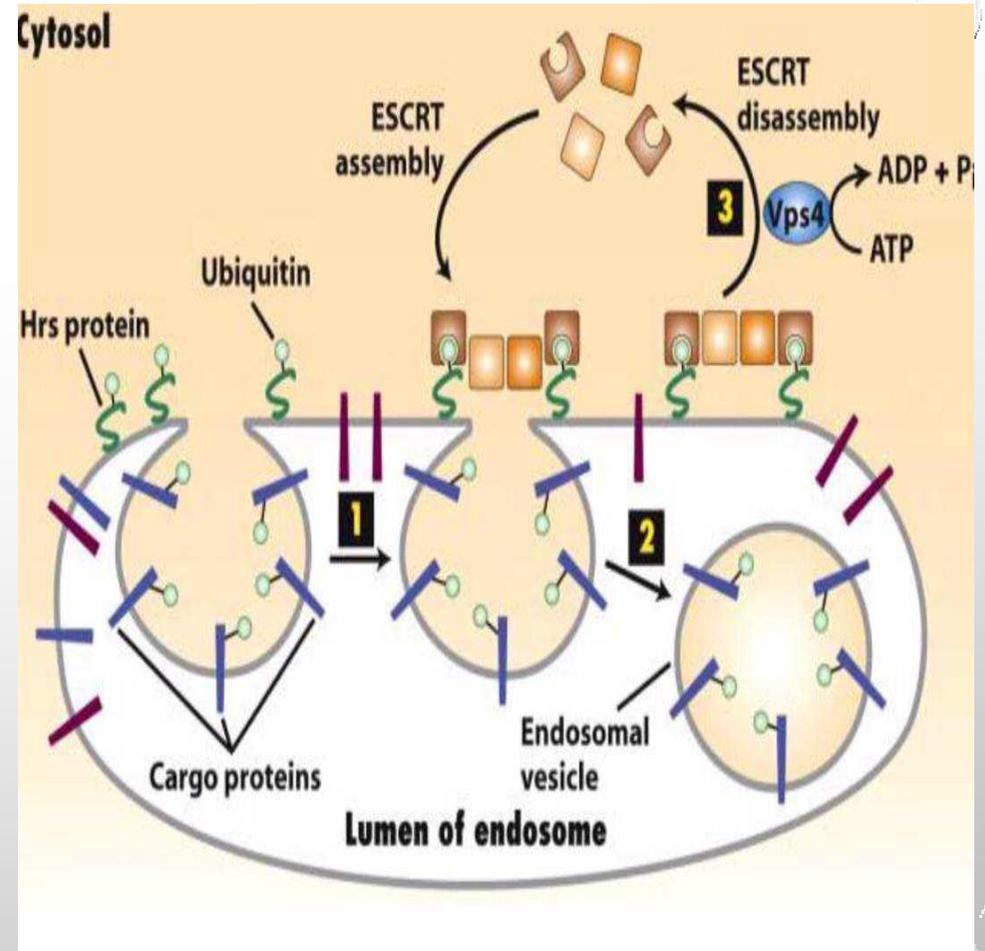
# EXOSOMES BIOGENESIS



# ESCRT COMPLEX

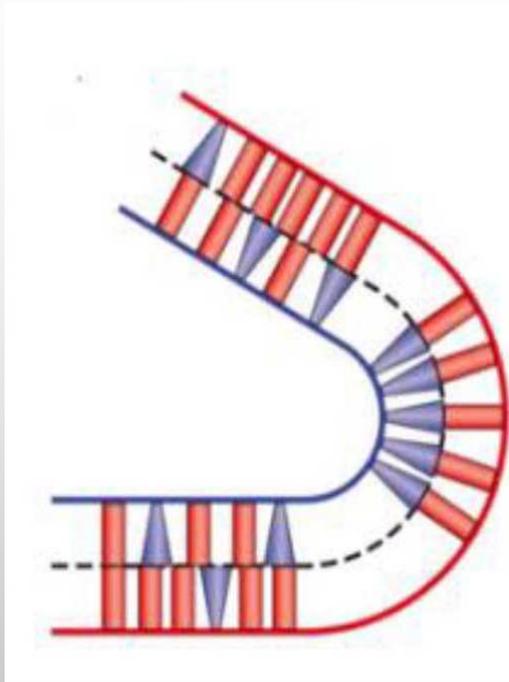


Phyllis I. Hanson, The Annual Review of Cell and Developmental Biology, 2012

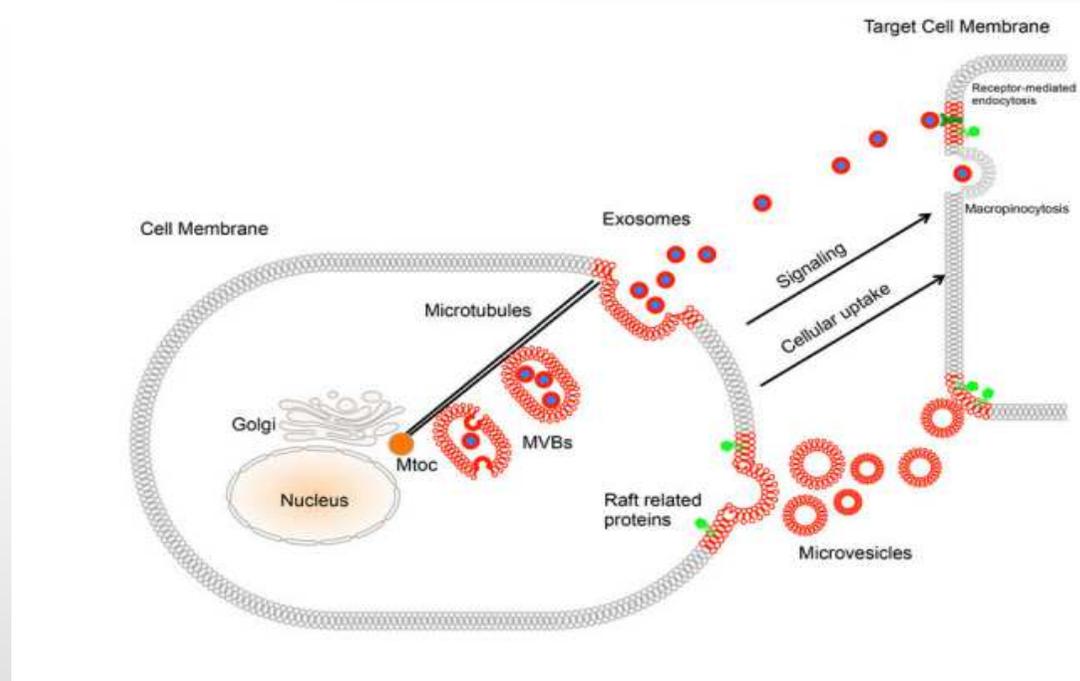


Valentina R. Minciacci, Journal of Semin Cell Dev Biol, 2016

# EXOSOME BIOGENESIS

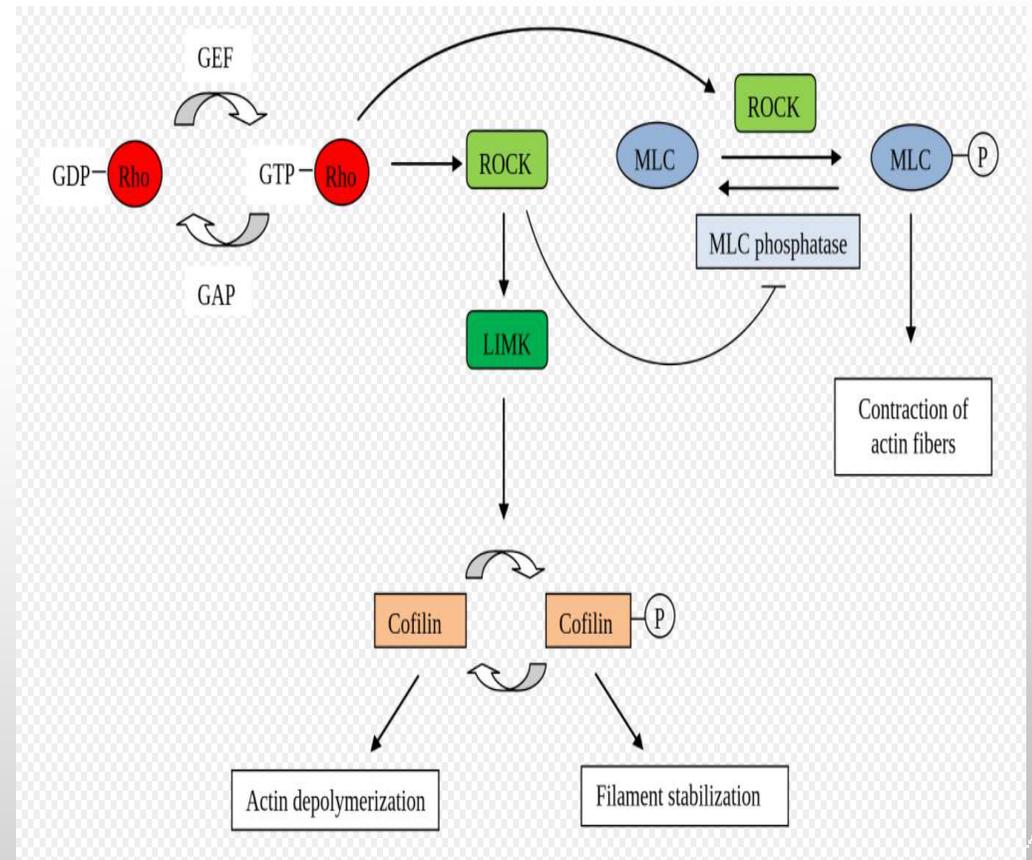
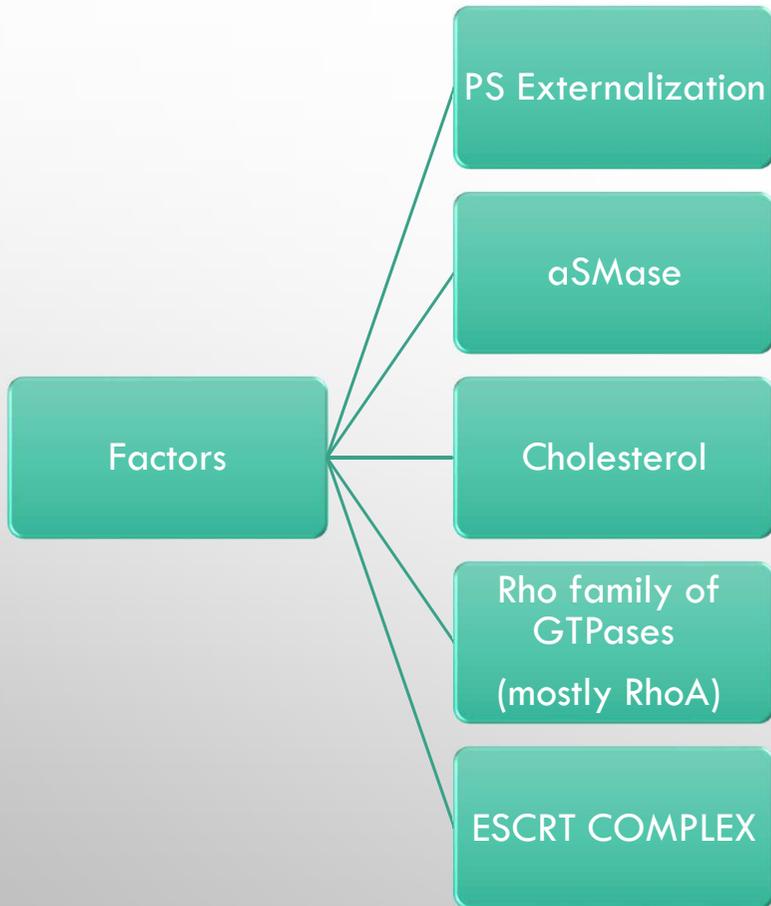


Ceramide structure ,  
Molecular Cell Biology,  
6<sup>TH</sup> EDITION,2007



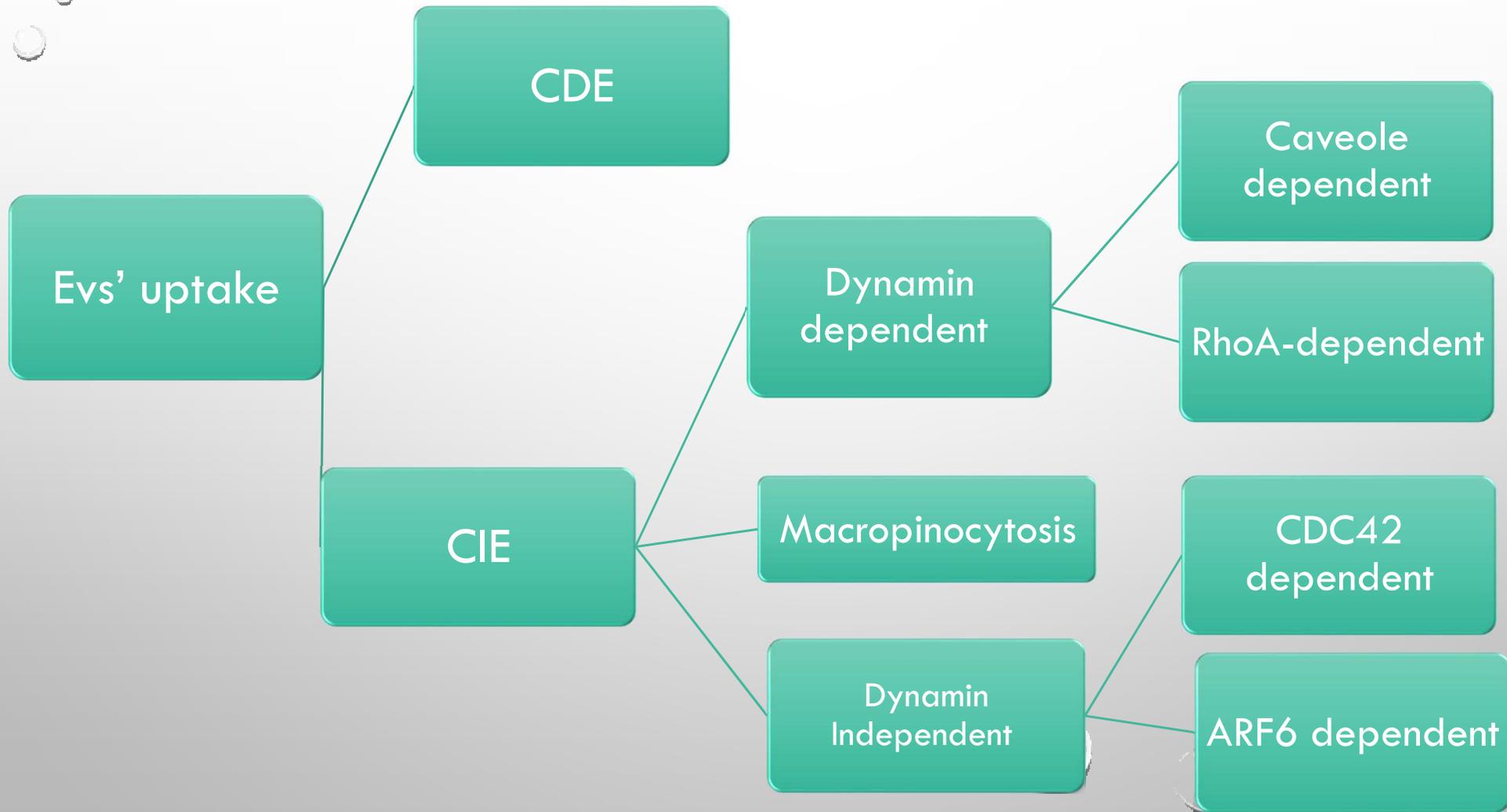
Contributions of cholesterol to the journey of Evs.  
Frank W. Pfrieger, Journal of Lipid Research,2018

# MVS BIOGENESIS

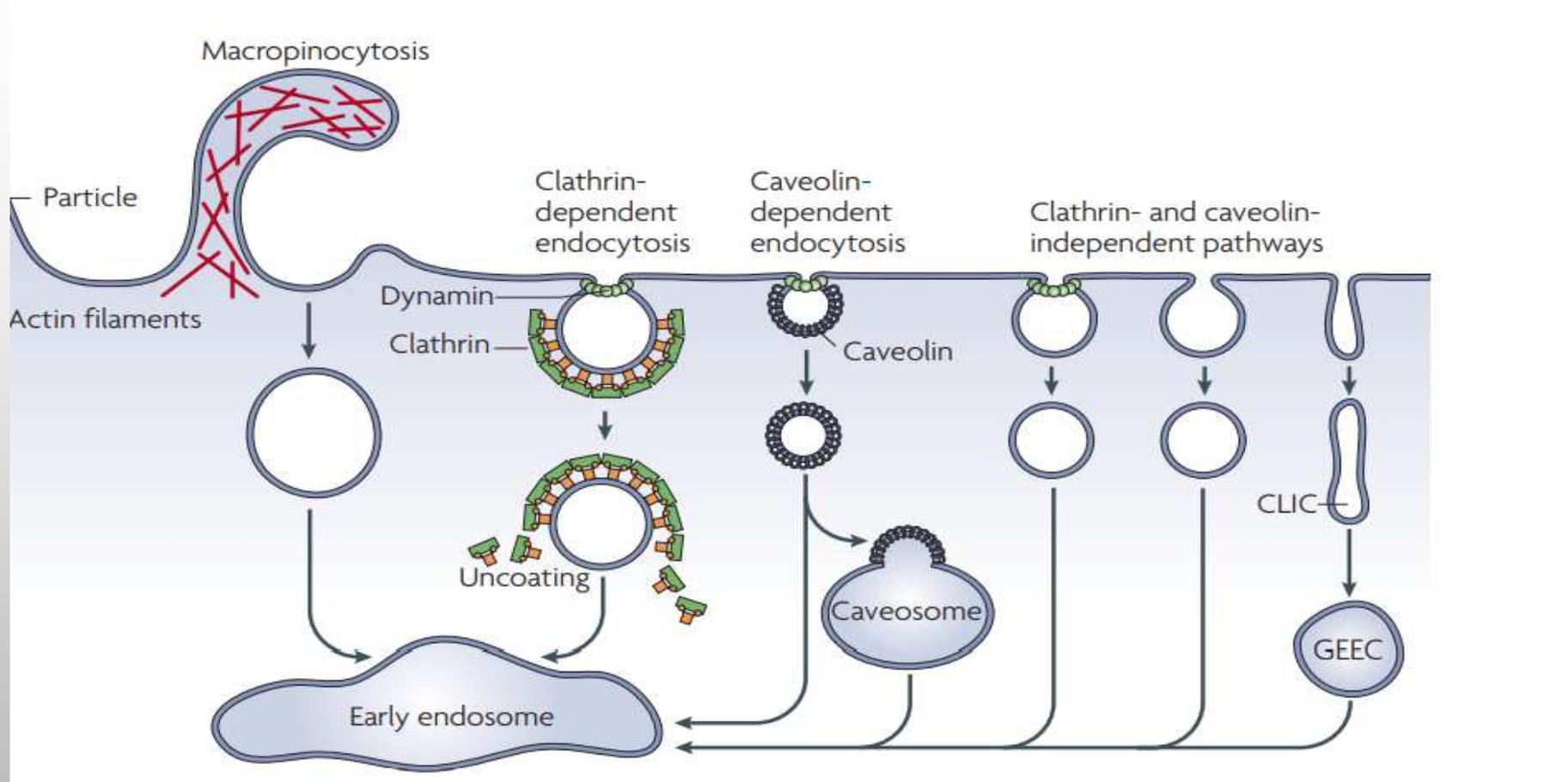


ROCK Role In MVs biogenesis.

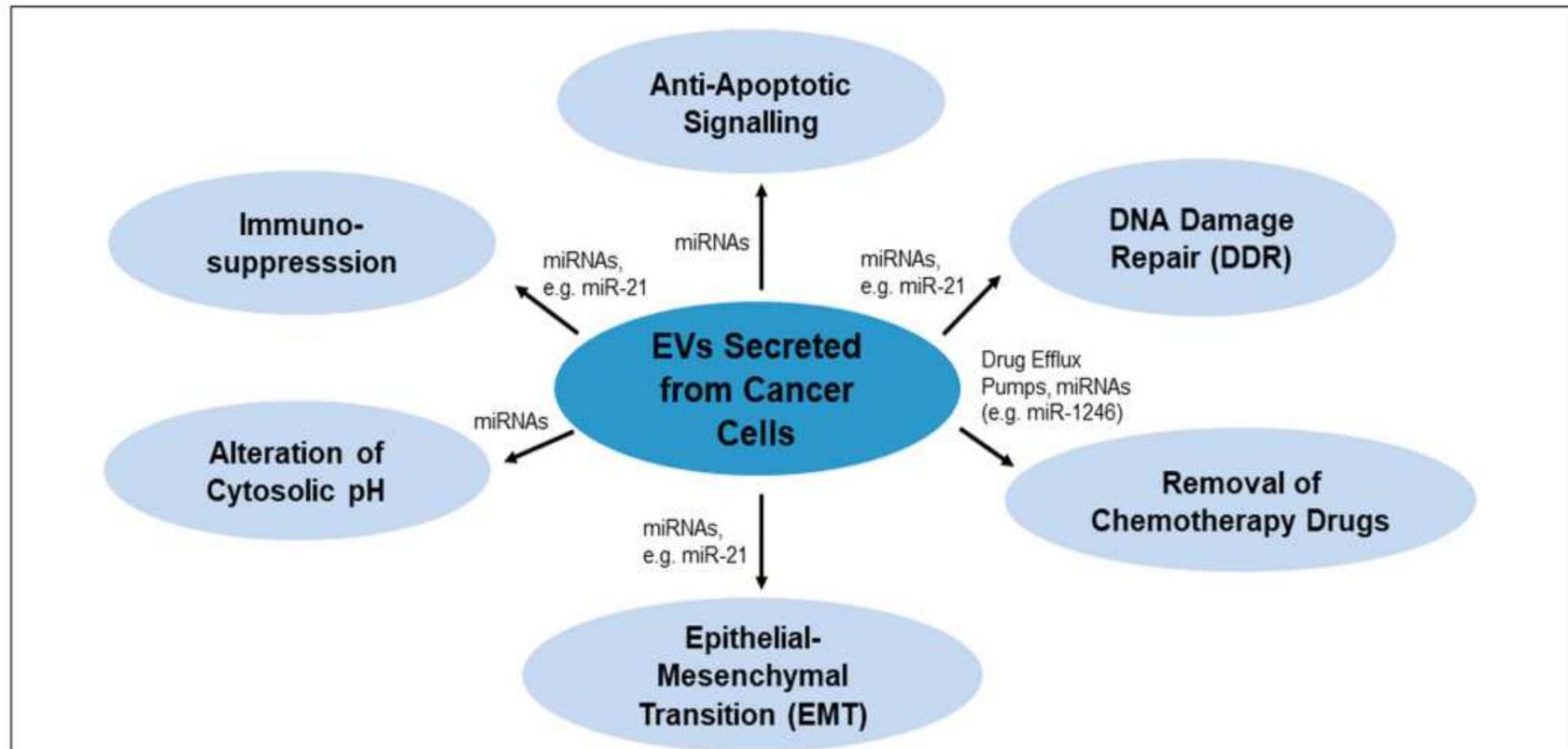
# UPTAKE OF EVS



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# REGULATION OF CHEMORESISTANCE BY EVS



**FIGURE 1** | Mechanisms of EVs-mediated chemoresistance miRNAs or proteins such as drug efflux pumps as the key players carrying drug resistance messages.

# INHIBITION OF EVS

## A. Lipid related pathways

- 1.Sphingomyelinases
- 2.PS translocation
- 3.ATP binding CASSETTE TRANSPORTERS OR OTHER PROTEINS WITHIN CELL

## B. Cytoskeletal organization

- 1.Actin interacting proteins
- 2.Other cytoskeleton related proteins

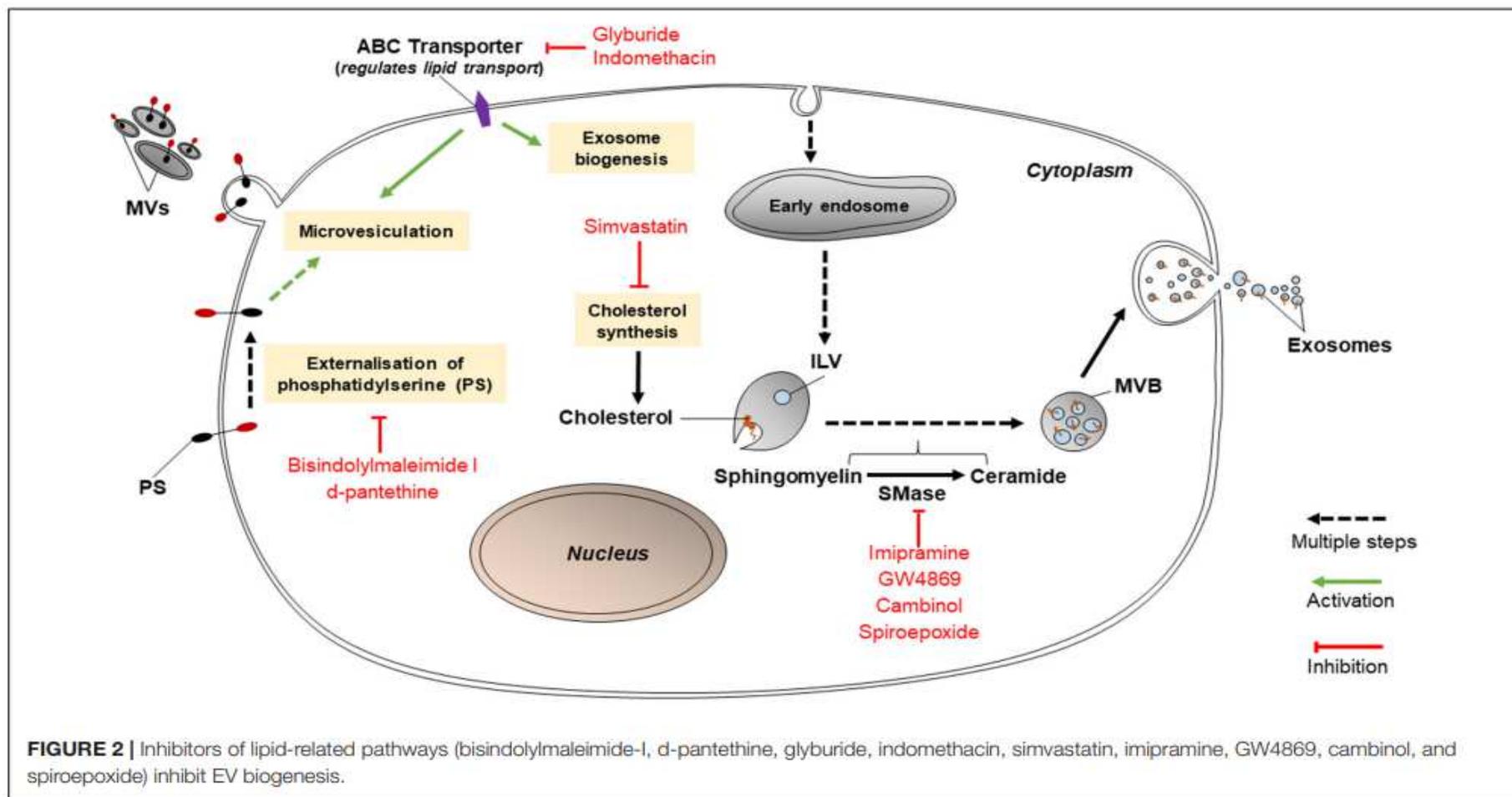
## C. EVs release

- 1.Protein kinases
- 2.ESCRT dependent pathways
- 3.Other pathways

## D. Endocytosis

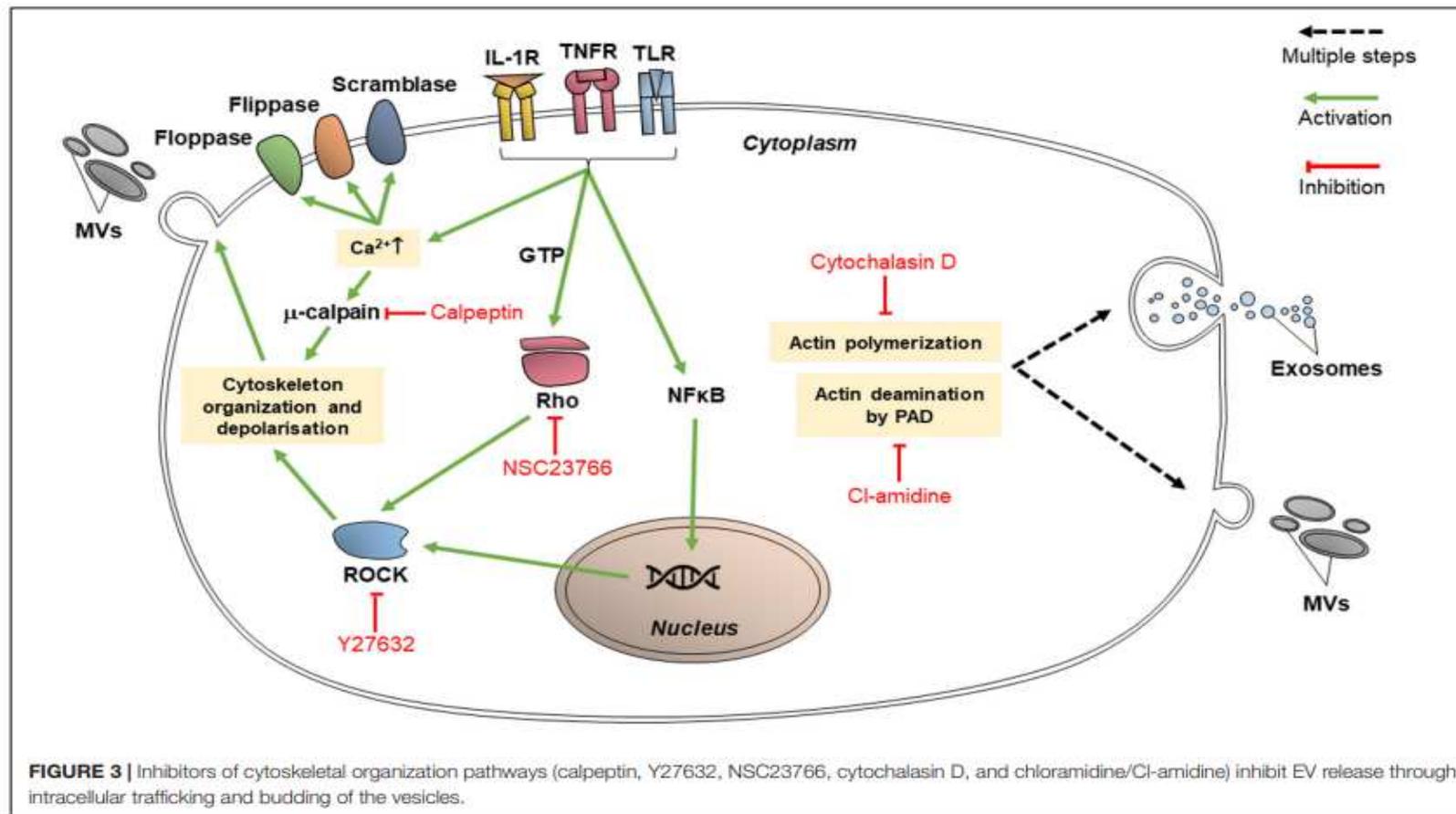
- 1.CDE
- 2.CIE

# Lipid related pathways

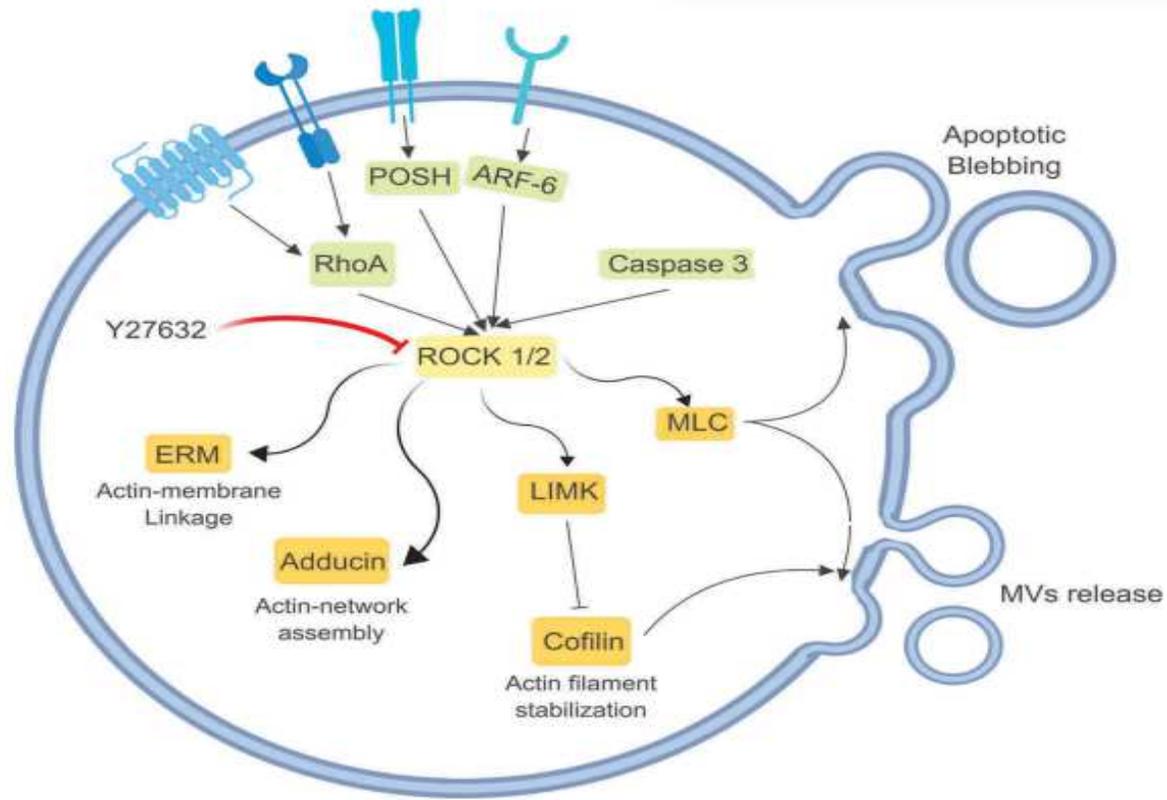




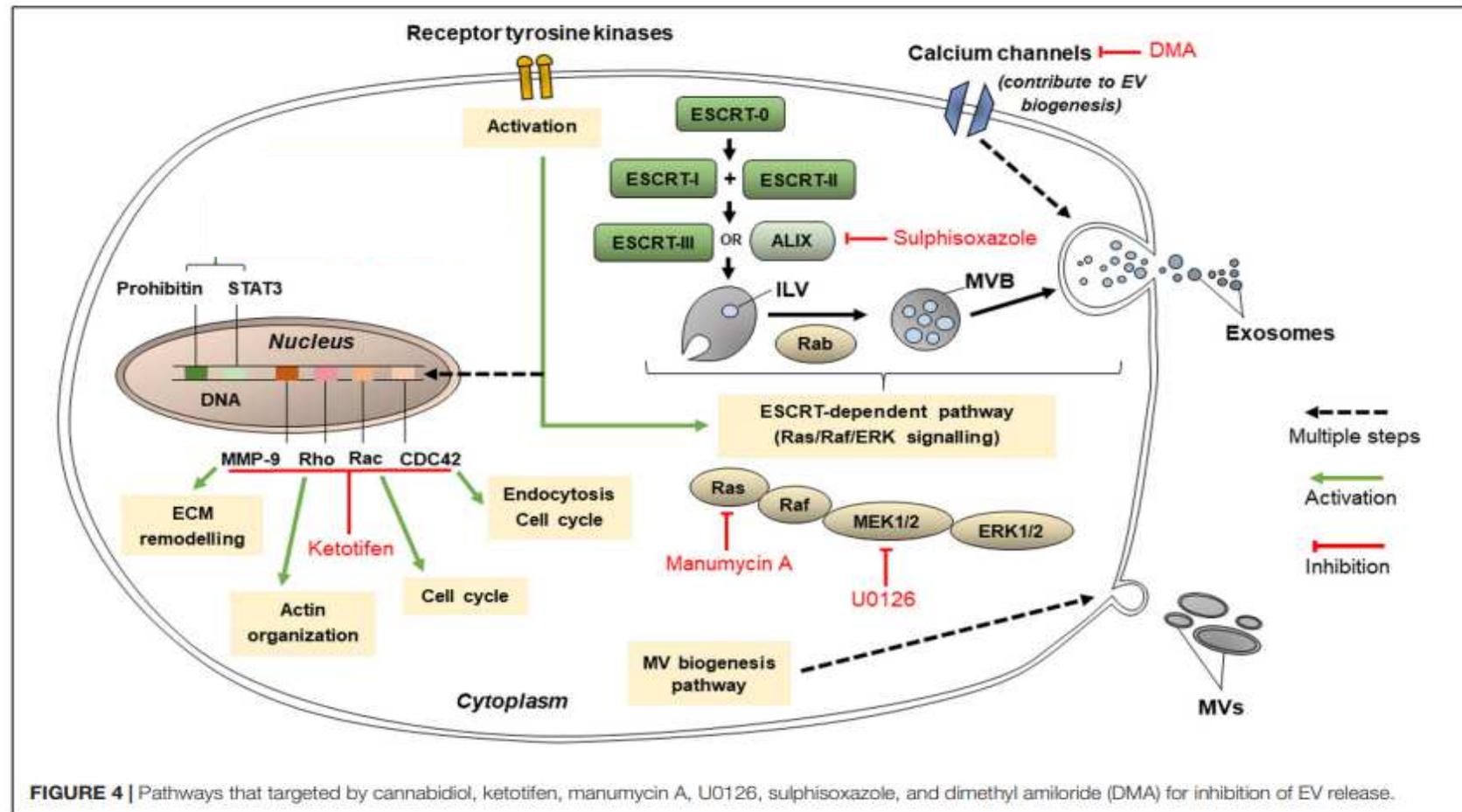
# CYTOSKELETAL ORGANIZATION



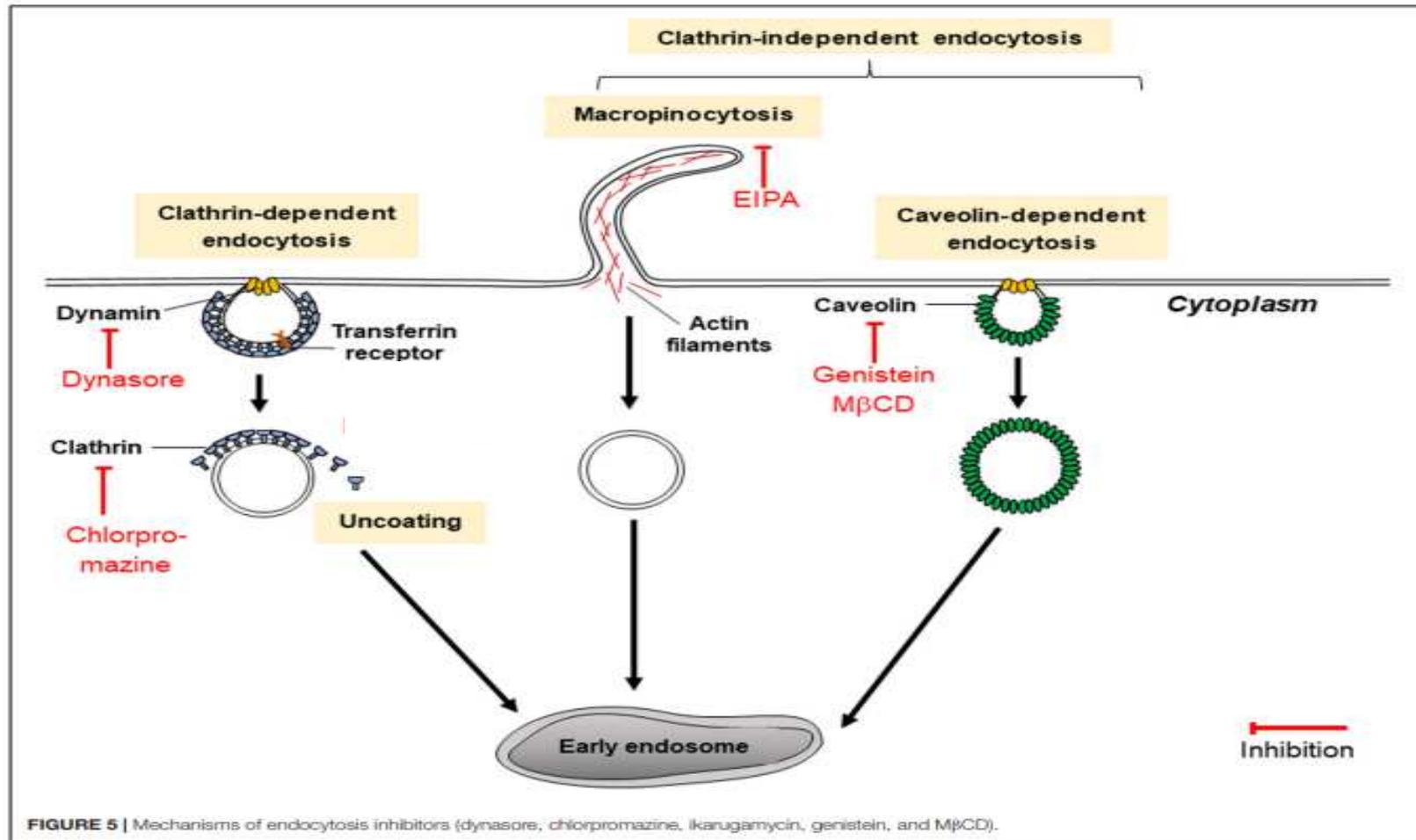
# CYTOSKELETAL ORGANIZATION



# EVS RELEASE



# ENDOCYTOSIS



# DIFFICULTIES, LIMITATIONS, AND CONSIDERATIONS IN EVS INHIBITION

Efficacy

Specificity

Toxicity

# TARGETING EVS IN CLINICAL APPLICATIONS

DMA+Cyclophosmide

Genetic Approach

Remove EVs from  
circulation in breast  
cancer



Thank You  
For Your  
Attention